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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,100	04/15/2004	Denis E. Ryono	LA0120 NP	9349

23914 7590 12/05/2006

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EXAMINER	
OH, TAYLOR V	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 12/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

TH

Office Action Summary	Application No.	Applicant(s)	
	10/826,100	RYONO ET AL.	
	Examiner	Art Unit	
	Taylor Victor Oh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2005*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-16* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

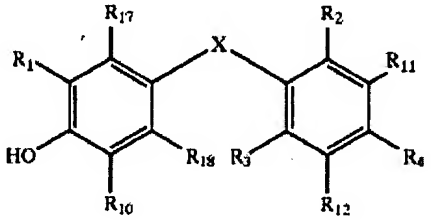
Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/05 & 9,10/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Election/Restriction

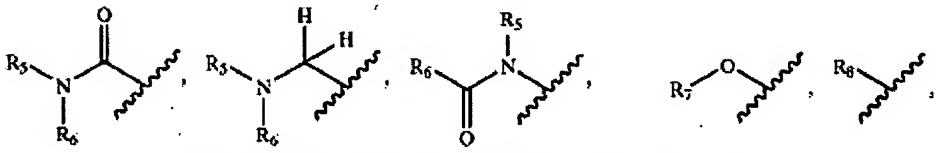
A. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-7,16 drawn to compounds of formula (I) with non-heterocyclic substituents as shown the formula (I) below:



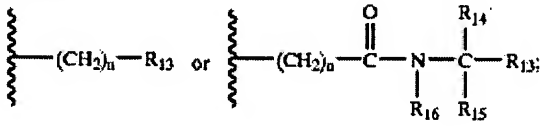
wherein:

R1 is



R2 and R3 are the same or different and are hydrogen, halogen, alkyl of 1 to 4 carbons or cycloalkyl of 3 to 5 carbons, provided that at least one of R2 and R3 is other than hydrogen;

R4 is



R5 and R6 are the same or different and are selected from hydrogen, aryl, alkyl, cycloalkyl, aralkyl;

R7 is aryl, . alkyl, aralkyl; R8 is aryl, or cycloalkyl;

R9 is R7 or hydrogen;

R10 is hydrogen, halogen, cyano or alkyl;

R11 and R12 are each independently selected from the group consisting of hydrogen, halogen, alkoxy, hydroxy (—OH) cyano, and alkyl;

R13 is carboxylic acid (COOH) or esters thereof, phosphonic and phosphinic acid or esters thereof,

sulfonic acid, hydroxamic acid, acylsulfonamide, or other carboxylic

acid surrogates known in the art;

R14 and R15 may be the same or different and are selected from hydrogen and alkyl, or R14 and R15 may be joined together forming a chain of 2 to 5 methylene groups [—(CH2)m-, m=2, 3, 4 or 5], thus forming 3- to 6-membered cycloalkyl rings;

R16 is hydrogen or alkyl of 1 to 4 carbons;

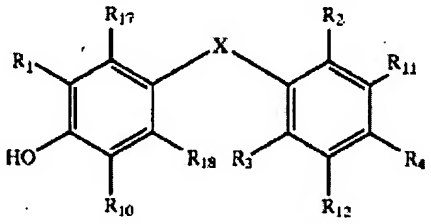
R17 and R18 are the same or different and selected from hydrogen, halogen and alkyl;

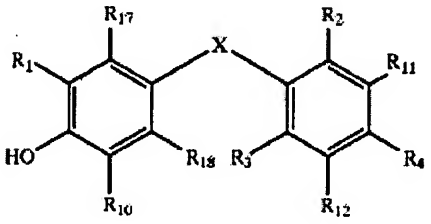
n is 0 or an integer from 1 to 4;

X is oxygen (—O—), sulfur (—S—), sulfonyl (—SO_2—), sulfenyl (—SO—) selenium (—Se—), carbonyl (—CO—), amino (—NH—) or methylene (—CH2-); wherein the substituents are as described herein.

and the pharmaceutical composition, classified in class 514, subclasses 522,617,615; class 558/410; class 564, subclasses 155,163.

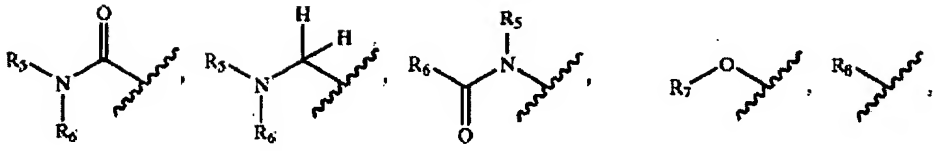
II. Claims 1-7 and 16, drawn to compounds of formula (I) of heterocyclic substituents,





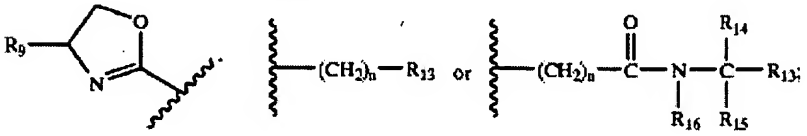
wherein:

R1 is



R2 and R3 are the same or different and are hydrogen, halogen, alkyl of 1 to 4 carbons or cycloalkyl of 3 to 5 carbons, provided that at least one of R2 and R3 is other than hydrogen;

R4 is



R5 and R6 are the same or different and are selected from heteroaryl, heteroaralkyl.;

R7 isheteroaryl,heteroaralkyl; R8 is heteroaryl,

R9 is R7 or hydrogen;

R10 is hydrogen, halogen, cyano or alkyl;

R11 and R12 are each independently selected from the group consisting of hydrogen, halogen, alkoxy, hydroxy (—OH) cyano, and alkyl;

R13 is tetrazole, thiazo- lidinedione;

R14 and R15 may be the same or different and are selected from hydrogen and alkyl, or R14 and R15 may be joined together forming a chain of 2 to 5 methylene groups [—(CH2)m-, m=2, 3, 4 or 5], thus forming 3- to 6-membered cycloalkyl rings;

R16 is hydrogen or alkyl of 1 to 4 carbons;

R17 and R18 are the same or different and selected from hydrogen, halogen and alkyl;

n is 0 or an integer from 1 to 4;

X is oxygen (—O—), sulfur (—S—), sulfonyl (—SO_2—), sulfenyl (—SO—) selenium (—Se—), carbonyl (—CO—), amino (—NH—) or methylene (—CH2-); wherein the substituents are as described herein.

and the pharmaceutical composition, classified in class 514, subclasses 357,374, 408; class 546, subclass 336; class 548, subclass 215.

III. Claim 8, drawn to a method for preventing , inhibiting or treating a disease associated with metabolism dysfunction, classified in class 514, subclasses 866 and 909.

IV. Claims 9-15, drawn to a method for treating or delaying the progression or onset of obesity, hypercholesterolemia, atherosclerosis, depression, osteoporosis, hypothyroidism, subclinical hyperthyroidism, non-toxic goiter, reduced bone mass, density or growth, eating disorders, reduced cognitive function, thyroid cancer, glaucoma, cardiac arrhythmia, congestive heart failure or a skin disease, classified in class 514, subclasses 886, 861, 821, and 913 .

1. **The inventions are distinct, each from the other because of the following reasons: Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case there are two different inventions I and II. The invention I is related to** compounds of formula (I) of non-heterocyclic substituents wherein moieties R1, R5,R6,R7, R8, R13 are selected from various non-hetero functional groups and their pharmaceutical composition**, whereas the invention II is related to** compounds of formula (I) of heterocyclic substituents, wherein moieties R1, R5, R6, R7, R8, R13 are substitutents selected from heteroaryl, heteroaralkyl, tetrazole, thiazolidinedione , various heterocylic groups and their pharmaceutical composition ; furthermore, the side chain groups of the heterocyclic compounds contain different kinds of heterocycles, such as furan, oxazole, 1,3-dioxane, thiophene,dioxa-borane, pyridine, pyrimidine, 1,3-thiazole, 1,2,3,4-tetrazole.

They have different structures and different functional groups in the ring, thereby exhibiting a chemically different activity respectively. Furthermore, they are classified in

different classes and subclasses; therefore, it is a burden for the examiner to search those broad classes and subclasses.

In addition, each invention has a different use and effect due to unrelated substituents attached to the core of the compounds.

If the applicants elect the invention I, the invention I is further subjected to the election species due to a plurality of disclosed patentably distinct species comprising compounds of formula I as shown in examples 1-168 in the specification.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, the compounds of formula I in the invention I are generic. Applicants are advised to elect one species among the examples in the specification.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims

are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

On the other hand, if the applicants elect the invention II, the invention II is further subjected to the restriction.

II. Claims 1-7,16, drawn to the heterocyclic containing various heterocycles further classified in the followings:

IIa. furan group in class 549 , subclass 429;

IIb. oxazole group in class 548, subclass 215;

IIc. 1,3-dioxane group in class 544, subclass 122;

IId. thiophene in class 544, subclass 146;

IIe.dioxa-borane in class 549, subclass 213;

IIf. pyridine in class 546, subclass 93;

IIg.pyrimidine in class 544, subclass 242;

IIh. 1,3-thiazole in class 548, subclass 215;

IIi. 1,2,3,4-tetrazole in class 548, subclass 250.

Inventions IIa, IIb, IIc, Iid IIe, IIf, IIg, Iih, and IIi are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01).

In the instant case, for an example, there are two different inventions IIa and IIb. The invention IIb is related to the side chain group of the heterocyclic compounds containing the oxazole group, whereas the invention IIa is related to the side chain group of the heterocyclic compounds containing furan group.

The oxazole group has one oxygen and one nitrogen in a five membered ring ,whereas the furan has one oxygen in a five membered ring. They have different structures and atoms in the ring, thereby exhibiting a chemically different activity respectively. Each invention has a different use and effect due to the unrelated substituent attached to the core of the compounds. Furthermore, they are classified in different subclasses; therefore, it is a burden for the examiner to search those subclasses.

In the instant case, for an example, there are two different inventions IIa and IIc. The invention IIa is related to the side chain group of the heterocyclic compounds containing furan group, whereas the invention IIc is related to the side chain group of the heterocyclic compounds containing the 1,3-dioxane group.

The furan has one oxygen in a five membered ring and the 1,3-dioxane group has a five-member-ring with two oxygens. They have different atoms in the ring, thereby exhibiting a chemically different activity respectively.

Each invention has a different use and effect due to the unrelated substituent attached to the core of the compounds. Furthermore, they are classified in different subclasses; therefore, it is a burden for the examiner to search those subclasses.

In the instant case, for an example, there are two different inventions IIa and IId. The invention IIa is related to the side chain group of the heterocyclic compounds containing furan group, whereas the invention IId is related to the side chain group of the heterocyclic compounds containing the thiophene group.

The furan has one oxygen in a five membered ring and the thiophene group has a five-member-ring with one sulfur. They have the different number of atoms in the ring, thereby exhibiting a chemically different activity respectively. Each invention has a different use and effect due to the unrelated substituent attached to the core of the compounds. Furthermore, they are classified in different subclasses; therefore, it is a burden for the examiner to search those subclasses.

In the instant case, for an example, there are two different inventions IIa and IIe. The invention IIa is related to the side chain group of the heterocyclic compounds containing the furan group , whereas the invention IIe is related to the side chain group of the heterocyclic compounds containing the dioxaborane group.

The furan group has a five-member-ring with one oxygen and the dioxaborane group has a five-member-ring with two oxygen and one borane. They have the different number of atoms in the ring, thereby exhibiting a chemically different activity respectively. Each invention has a different use and effect due to the unrelated substituent attached to the core of the compounds. Furthermore, they are classified in

different subclasses; therefore, it is a burden for the examiner to search those subclasses.

In the instant case, for an example, there are two different inventions IIa and IIf. The invention IIa is related to the side chain group of the heterocyclic compounds containing the furan group , whereas the invention IIf is related to the side chain group of the heterocyclic compounds containing the pyridine group.

The pyridino group has a six-member-ring with one nitrogen and the furan group has a five-member-ring with oxygen. They have the different number of atoms in the ring, thereby exhibiting a chemically different activity respectively. Each invention has a different use and effect due to the unrelated substituent attached to the core of the compounds. Furthermore, they are classified in different subclasses; therefore, it is a burden for the examiner to search those subclasses.

In the instant case, for an example, there are two different inventions IIa and IIg. The invention IIa is related to the side chain group of the heterocyclic compounds containing the furan group , whereas the invention IIg is related to the side chain group of the heterocyclic compounds containing the pyrimidine group.

The pyrimidine group has a six-member-ring with two nitrogens and the furan group has a five-member-ring with oxygen. They have the different number of atoms in the ring, thereby exhibiting a chemically different activity respectively. Each invention has a different use and effect due to the unrelated substituent attached to the core of the compounds. Furthermore, they are classified in different subclasses; therefore, it is a burden for the examiner to search those subclasses.

In the instant case, for an example, there are two different inventions IIa and IIh. The invention IIa is related to the side chain group of the heterocyclic compounds containing the furan group , whereas the invention IIh is related to the side chain group of the heterocyclic compounds containing the 1,3-thiazole group.

The 1,3-thiazole has a five-member-ring with one sulfur and one nitrogen and the furan group has a five-member-ring with oxygen. They have the different number of atoms in the ring, thereby exhibiting a chemically different activity respectively. Each invention has a different use and effect due to the unrelated substituent attached to the core of the compounds. Furthermore, they are classified in different subclasses; therefore, it is a burden for the examiner to search those subclasses.

In the instant case, for an example, there are two different inventions IIa and IIi. The invention IIa is related to the side chain group of the heterocyclic compounds containing the furan group , whereas the invention IIi is related to the side chain group of the heterocyclic compounds containing the 1,2,3,4-tetrazole group.

The 1,2,3,4-tetrazole has a five-member-ring with four nitrogens and the furan group has a five-member-ring with oxygen. They have the different number of atoms in the ring, thereby exhibiting a chemically different activity respectively. Each invention has a different use and effect due to the unrelated substituent attached to the core of the compounds. Furthermore, they are classified in different subclasses; therefore, it is a burden for the examiner to search those subclasses.

Similarly, the rest of other groups can be differentiated (e.i. among other groups IIb and Iic-IIi).

Furthermore, If the applicants elect the invention II, the invention II is further subjected to the election species due to a plurality of disclosed patentably distinct species comprising compounds of formula I as shown in examples 1-168 in the specification.

2. The inventions are distinct, each from the other because of the following reasons: Inventions III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case there are two different inventions I and II. The invention III is related to the method for preventing , inhibiting or treating a disease associated with metabolism dysfunction, **whereas the invention IV is related to** the method for treating or delaying the progression or onset of obesity, hypercholesterolemia, atherosclerosis, depression, osteoporosis, hypothyroidism, subclinical hyperthyroidism, non-toxic goiter, reduced bone mass, density or growth, eating disorders, reduced cognitive function, thyroid cancer, glaucoma, cardiac arrhythmia, congestive heart failure or a skin disease.

They have different modes of operation, different functions, or different effects because of the difference in the treatments or their causative factors between the two inventive groups; for example, **the invention III is** the disease associated with metabolism dysfunction, whereas **the invention IV is** the diseases un-associated with metabolism dysfunction , such as depression, osteoporosis, reduced cognitive function, glaucoma, cardiac arrhythmia, congestive heart failure or a skin disease. Furthermore, they are classified in different classes and subclasses; therefore, it is a burden for the examiner to search those broad classes and subclasses.

3. The inventions are distinct, each from the other because of the following reasons: Inventions I and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case there are two different inventions I and III. The invention III is related to the method for preventing , inhibiting or treating a disease associated with metabolism dysfunction using the compounds of formula (I), whereas the invention I is related to the compounds of formula (I) with non-heterocyclic substituents. They are unrelated to each other because Schafer et al (US 6,930,103) discloses vasopeptidase inhibitors in the treatment of metabolic diseases, which is totally unassociated with using the compounds of formula (I). Thus, there are unrelated to each other.

4. The inventions are distinct, each from the other because of the following reasons: Inventions I and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case there are two different inventions I and IV. The invention IV is related to the method for treating or delaying the progression or onset of obesity, hypercholesterolemia, atherosclerosis, depression, osteoporosis, hypothyroidism, subclinical hyperthyroidism, non-toxic goiter, reduced bone mass, density or growth, eating disorders, reduced cognitive function, thyroid cancer, glaucoma, cardiac arrhythmia, congestive heart failure or a skin disease.

Whereas the invention I is related to the compounds of formula (I) with non-heterocyclic substituents. They are unrelated to each other because Donovan (US

6740321) discloses the method for treating thyroid disorders with a botulinum toxin, which is totally unassociated with using the compounds of formula (I). Thus, there are unrelated to each other.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

6. Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

7. A telephone call was made to Jonathan N. Provoost on 11/29/06 to request an oral election to the above restriction requirement, but did not result in an election being made.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TAYLOR VICTOR OH, MSD, LAC
Primary Examiner
Art unit : 1625

11/29/05

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